

Revised Abstract

Background: Successful treatment of infections due to *Pseudomonas aeruginosa* has become problematic due to widespread resistance to currently available therapies. Since many isolates exhibit resistance to multiple antimicrobial agents, older agents, such as colistin (polymyxin E), are being reexamined for their treatment potential. This study investigated the activity of colistin against European clinical isolates of *P. aeruginosa* collected during 2009 - 2010. **Methods:** 504 *P. aeruginosa* isolates collected from 25 European countries during the 2009-2010 Tigecycline European Surveillance Trial (TEST) from various infection sources were included in this study. MICs were performed following CLSI guidelines and interpreted according to EUCAST breakpoints.

Results:

	MIC ₅₀ (mg/L)	MIC ₉₀ (mg/L)	%S ^a	%I	%R
Colistin	2	4	97.8	nd	2.2
Cefepime	4	32	75.8	nd	24.2
Imipenem	2	>16	72.2	4.4	23.4
Meropenem	0.5	16	72.2	14.1	13.7
PipTazo	8	>128	65.9	nd	34.1
Ceftazidime	8	>32	61.7	nd	38.3
Levofloxacin	1	>8	54.2	10.5	35.3

^aInterpretive criteria are defined according to EUCAST breakpoints, 2011; nd=not defined breakpoint

Conclusions: Colistin was the most active agent *in vitro*, with 97.8% of *P. aeruginosa* isolates, including multi-drug resistant strains (97.7%), susceptible by EUCAST criteria. Colistin represents a potential addition to the treatment of drug-resistant *P. aeruginosa*. As usage of this agent increases, careful monitoring of the incidence of resistance is warranted.

Introduction

Pseudomonas aeruginosa is a gram-negative bacillus that is ubiquitous in the environment. In humans, it is responsible for chronic lung infections in patients with cystic fibrosis as well as serious acute infections in immunocompromised individuals, and is a common cause of ventilator-associated pneumonia and septic burn wounds [1]. Worldwide, *P. aeruginosa* is the third leading cause of nosocomial infections [2]. Successful treatment of infections due to *P. aeruginosa* has become problematic due to widespread resistance to currently available therapies. Since many isolates exhibit resistance to multiple antimicrobial agents, older agents, such as colistin (polymyxin E), are being reexamined for their treatment potential [3-5]. This study investigated the activity of colistin against European clinical isolates of *P. aeruginosa* collected in the TEST program during 2009 - 2010.

Materials & Methods

➤ All TEST study isolates were derived from blood, respiratory tract, urine, skin, wound, body fluids and other defined sources. Only one isolate per patient was accepted into the study. Clinical isolates were collected between 2009 and 2010 from hospitals from 25 European countries.

➤ Organism collection, transport, confirmation of organism identification, as well as development and management of a centralized database was coordinated by Laboratories International for Microbiology Studies (LIMS), a division of International Health Management Associates, Inc. (IHMA) located in Schaumburg, IL, USA.

➤ Minimum inhibitory concentrations (MICs) were determined by the CLSI recommended broth microdilution testing method [6] on panels produced at IHMA. MIC interpretive criteria followed published guidelines established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) [7].

➤ Quality controls (QC) were performed by each testing site on each day of testing using the corresponding ATCC control strains *Escherichia coli* ATCC 25922, *E. coli* ATCC 35218, and *P. aeruginosa* ATCC 2785. Results were included in the analysis only when corresponding QC isolates tested within the acceptable range according to CLSI guidelines [8].

References

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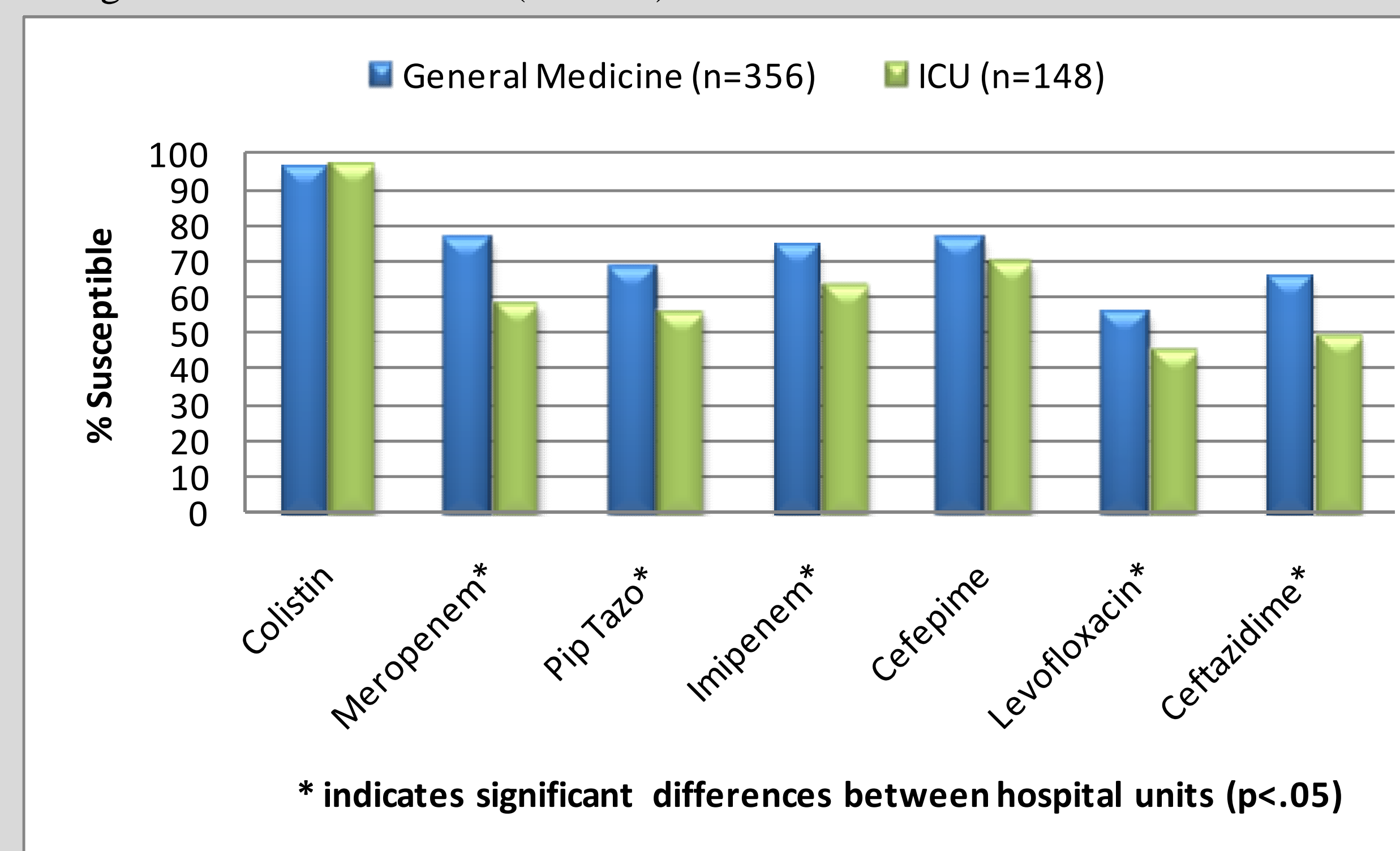
Results

Table 1. *In vitro* activity of colistin and comparators against 504 *P. aeruginosa* from Europe, 2009-2010.

	MIC ₅₀ (mg/L)	MIC ₉₀ (mg/L)	%S ^a	%I	%R
Colistin	2	4	97.8	nd	2.2
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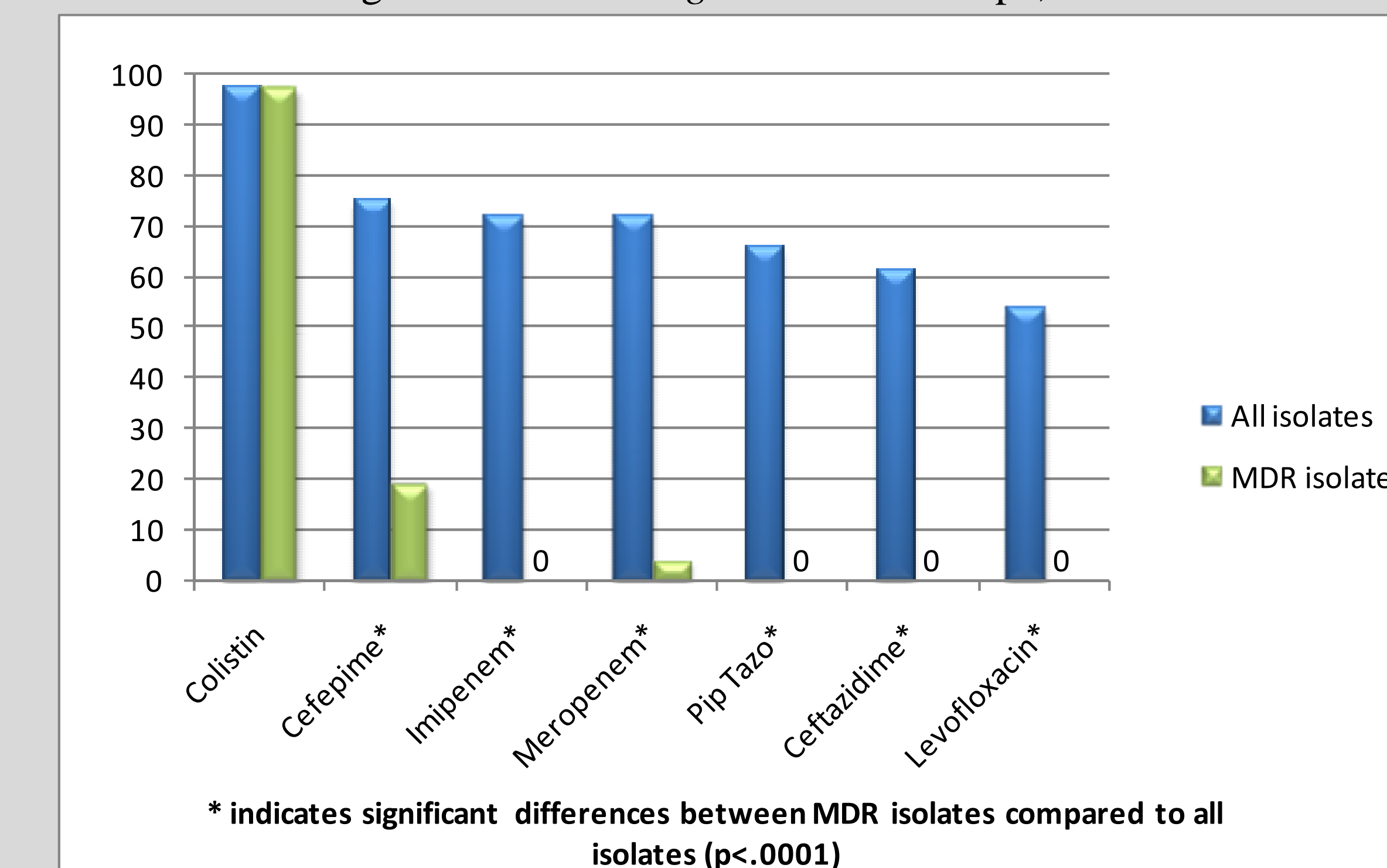
Figure 2. Susceptibility^a of *P. aeruginosa* from European Intensive Care Units (ICU; n = 148) and general medicine wards (n = 356).



^aInterpretive criteria are defined according to EUCAST breakpoints, 2011

* indicates significant differences between hospital units (p<.05)

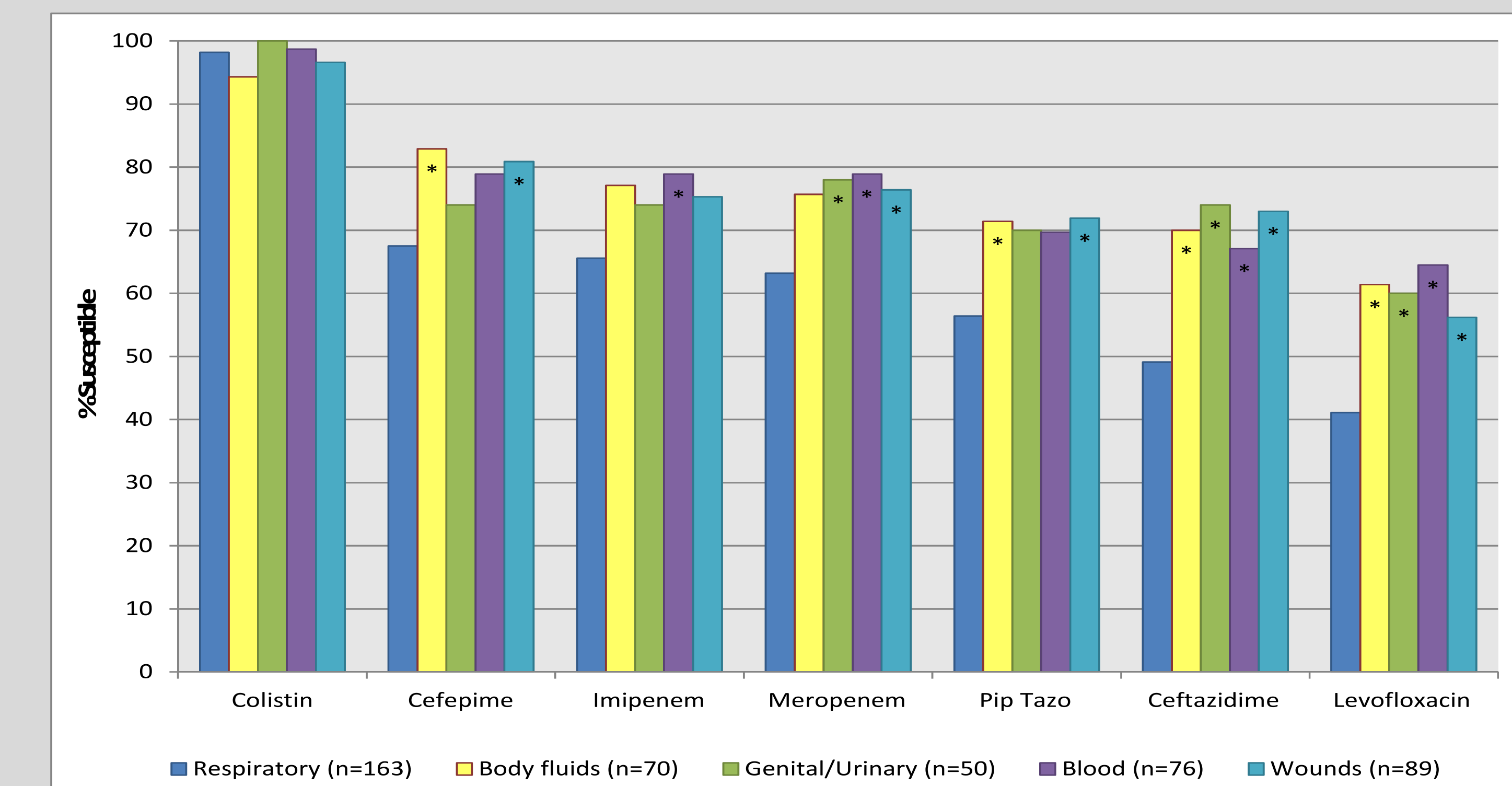
Figure 1. *In vitro* activity of colistin and comparators against 504 *P. aeruginosa* from Europe and 88 multi-drug resistant^a *P. aeruginosa* from Europe, 2009-2010.



^aMulti-drug resistance defined as resistant to 3 or more drug classes

* indicates significant differences between MDR isolates compared to all isolates (p<.0001)

Figure 3. Susceptibility^a of isolates of *P. aeruginosa* from Europe from defined body sites, 2009-2010.



^aInterpretive criteria are defined according to EUCAST breakpoints, 2011

* indicates a significant difference between isolates from that body site and respiratory isolates (p<.05)

Conclusions

- Colistin was the most active agent *in vitro*, with 97.7% of European *P. aeruginosa* isolates in this study, including multi-drug resistant strains, susceptible by EUCAST criteria (MIC <4 mg/L).
- With the exception of colistin and cefepime, all agents showed significant differences between the susceptibility of isolates from ICUs and general medicine units (p<.05).
- There were no significant differences in colistin activity against isolates from different body sites. All other agents showed some significant differences between respiratory isolates versus isolates from other sources (p<.05).
- While colistin represents a potential addition to the treatment of drug-resistant *P. aeruginosa*, careful monitoring of the incidence of resistance will be necessary as usage of this agent increases.